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## ORIGINAL ARTICLE

# Risk factors associated with prolonged postoperative ileus after elective colon resection<sup>☆</sup>



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### KEYWORDS

Prolonged ileus;  
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### Abstract

**Background:** There is a coordinated inhibition of motility of the colon after its surgical manipulation that contributes to the accumulation of fluids and gas, in turn characterized by nausea, vomiting, pain, abdominal distension, and constipation. Motility is recovered in the majority of patients within the first 72 hours. A delay in its resolution is known as prolonged postoperative ileus.

**Aims:** To study the preoperative, intraoperative, and postoperative risk factors for developing prolonged ileus in patients that underwent elective colon resection.

**Materials and methods:** The association between 25 perioperative variables and the presentation of prolonged ileus was analyzed in 85 patients that underwent colon resection at *Hospital Christus Muguerza Alta Especialidad* within the time frame of 2011 and 2014.

**Results:** Postoperative ileus occurred in 22.3% of the patients. The statistically significant predictors of ileus were obesity (OR 1.119,  $P=.048$ ) and admission to the intensive care unit (OR 3.571,  $P=.050$ ). The use of peridural anesthesia during the surgical act was found to be a protective factor (OR 0.363,  $P=.050$ ).

**Conclusions:** The presence of these risk factors can alert the physician to the need for a closer follow-up in patients at high risk for postoperative ileus, and the use of peridural anesthesia can possibly lower the incidence of ileus.

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**PALABRAS CLAVE**

Íleo prolongado;  
Resección colónica;  
Factores de riesgo

## Factores de riesgo asociados a íleo posquirúrgico prolongado en pacientes sometidos a resección electiva de colon

**Resumen**

**Antecedentes:** Posterior a la manipulación quirúrgica del colon, existe una inhibición coordinada de su motilidad; esto contribuye al acúmulo de secreciones y gas que, a su vez, provocan náuseas, vómito, dolor, distensión abdominal y estreñimiento. La mayoría de los pacientes recupera la motilidad dentro de las primeras 72 h; el retraso en su aparición se denomina íleo posquirúrgico prolongado.

**Objetivos:** Investigar los factores de riesgo pre, intra y postoperatorios para el desarrollo de íleo prolongado en pacientes sometidos a resección electiva de colon.

**Materiales y métodos:** Se analizarán 25 variables perioperatorias de 85 pacientes sometidos a resección colónica entre los años 2011 y 2014 en el Hospital Christus Muguerza Alta Especialidad y su relación con la aparición de íleo prolongado.

**Resultados:** El íleo posquirúrgico se presentó en 22.3% de los pacientes. Se encontró significación estadística como predictor de íleo: la presencia de obesidad (OR 1.119,  $p = 0.048$ ) y el ingreso a terapia intensiva (OR 3.571,  $p = 0.050$ ). Como factor protector se encontró el uso de anestesia peridural durante el acto quirúrgico (OR 0.363,  $p = 0.050$ ).

**Conclusiones:** La presencia de estos factores de riesgo pueden servir como alertas para un seguimiento más cercano en pacientes de alto riesgo de íleo postoperatorio. El uso de anestesia peridural pudiera disminuir la incidencia de íleo.

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**Introduction**

After its surgical manipulation, each part of the gastrointestinal tract recovers its normal motility at different times, on average: the small bowel in the first 12 h, the stomach in the first 24 to 48 h, and the colon in 3 to 5 days. In the postoperative period, some patients present with an inhibition of the coordinated activity of the gastrointestinal tract which contributes to the accumulation of fluids and gas that in turn causes nausea, vomiting, abdominal distension, and constipation. This is traditionally defined as postoperative ileus and is the most common cause of delayed hospital release in the United States.<sup>1,2</sup>

Gastrointestinal tract motility is controlled by 3 different nervous systems: the parasympathetic, sympathetic, and intrinsic. The parasympathetic system increases motility, whereas the activation of the sympathetic system decreases it. Unlike the most proximal segments, the cellular configuration of the colon conditions less coordination of its motility, making it practically independent from the rest of the gastrointestinal tract; its motility depends mainly on the presence of content and on its extrinsic innervation. Surgical stress conditions a sustainedly increased sympathetic tone.<sup>1</sup>

The release of inflammatory mediators also contributes to the development of postoperative ileus. Intestinal manipulation conditions an increase in vascular permeability, inflammatory cell migration to the muscle layer, and augmented production of nitric oxide, prostaglandins, vasoactive intestinal peptide, calcitonin, and substance P. Other theoretical mechanisms are: the release of endogenous substances by the intestinal bacteria,<sup>1</sup> postoperative pain, overhydration, the administration of general anesthesia, and the use of opioid analgesics.<sup>2,3</sup>

The diagnosis of prolonged postoperative ileus is eminently clinical, given that there is no laboratory or imaging study that confirms or excludes it. The usefulness of radiologic studies is evident when mechanical obstruction or some other specific cause is suspected.<sup>3</sup> The endpoints that are traditionally used in studies that investigate the resolution of postoperative ileus are subjective: the return of peristalsis, first bowel movement, and tolerance of oral diet.<sup>2,3</sup> Currently, there is no internationally accepted definition, and thus its incidence is estimated at between 3 and 32% of the cases of major abdominal surgery.<sup>4,5</sup>

Vather et al. (2013) recently published a meta-analysis of 52 publications and proposed the definitions of "normal postoperative ileus" and "prolonged postoperative ileus":<sup>4</sup>

- Normal postoperative ileus: absence of passage of flatus/stool or inability to tolerate oral diet before the fourth postoperative day.
- Prolonged postoperative ileus: 2 or more of the following criteria after the fourth postoperative day:
  - Nausea or vomiting.
  - Inability to tolerate oral diet.
  - Absence of passage of flatus or stool.
  - Abdominal distension.
  - Radiologic confirmation.

The aim of our study was to investigate the preoperative, intraoperative, and postoperative risk factors for the development of prolonged postoperative ileus in patients that underwent elective colon resection due to any cause, and to identify the most useful factors in its prevention.

## Methods

A retrospective, observational, cross-sectional, and analytic study was conducted on all the patients above 16 years of age that underwent elective colon resection due to any cause within the time frame of March 2011 and September 2014 at the *Hospital Christus Muguerza Alta Especialidad*, a private tertiary care hospital in the northeast of Mexico. All the surgeries were performed by general or colorectal surgeons affiliated with the medical staff of the hospital.

The variables included were: sex, age, body mass index, previous abdominal surgeries, and the classification of surgical risk according to the American Society of Anesthesiologists (ASA); also included were the comorbidities of heart disease, smoking, diabetes mellitus, high blood pressure, chronic obstructive pulmonary disease, and prior treatment with chemotherapy or radiotherapy.

With respect to the surgical procedure, the following elements were documented: days of hospital stay, preoperative hemoglobin values, procedure indication (malignancy vs benign disease), type of procedure, conventional vs laparoscopic approach, estimated surgery duration, estimated anesthesia duration, estimated blood loss, intraoperative transfusions, and the use of intraoperative opioids (expressed in milliequivalents of morphine).

The documented postoperative variables were the time of the first passage of flatus, time of the first passage of stool, time of appearance of peristalsis, and time of toleration of oral diet. The documented postoperative management variables were the use of parenteral nutrition, prokinetics, opioid analgesics or nonsteroidal anti-inflammatory drugs (NSAIDs), anti-thrombotic prophylaxis, and the need for intensive care management.

A total of 95 patients were found during the study period and they were distributed as follows: 2011, 20 (21%); 2012, 16 (18%); 2013, 32 (33%); and 2014, 24 (26%). The decision was made to calculate a significant sample with a 5% percentage of error and a 95% confidence interval, which resulted in 76 cases. Complete information was obtained for 89 patients (93%) and 4 patients were excluded due to early complication or death. The final analysis included 85 patients, conferring a significance level on the sample that was close to 99%.

The register of values, formula calculations, graphs, conversions, and result interpretations were performed using the Microsoft Excel 2013 program. The inferential statistical analysis was carried out with MedCalc Statistical Software version 14.8.1.

The definition we used for prolonged postoperative ileus followed the recommendations published by Vather et al. (2013): the absence of passage of flatus/stool or inability to tolerate oral diet  $\geq 4$  postoperative days. The sample was divided into 2 groups (ileus/non-ileus) and odds ratio (OR) tests were performed to validate each variable as a risk factor for prolonged postoperative ileus. The values were expressed as crossed products and 95% confidence intervals. Chi-square tests were also carried out for statistical significance and the Fisher's exact test was used for the variables that had values below 5.

Some of the continuous variables were converted to discrete dichotomies to facilitate their analysis:

- BMI: presence or absence of obesity ( $\text{BMI} \geq 30$ ).
- Surgery duration: duration longer or not longer than 180 min.
- Anesthesia duration: duration longer or not longer than 180 min.
- Intraoperative bleeding: blood loss approximately greater or less than 500 ml.
- Preoperative hemoglobin level: presence or absence of anemia ( $M < 13$ ,  $W < 12$  g/dl).

The present study identified the administration of only 2 narcotic medications: fentanyl and sufentanil. They are both morphine derivatives and the values were converted to morphine equivalents to facilitate their analysis. The following conversion parameters were used:

- Fentanyl: conversion factor of 0.1.
- Sufentanil: conversion factor of 1.

All statistically significant cases had a  $p \leq 0.05$ .

## Results

### Population characteristics

Table 1 shows the clinical characteristics of the 85 patients studied. No perioperative mortality in the patients was reported. The study population presented with a higher frequency of women (58%) and a  $\text{BMI} < 30$ . Approximately 20% of the population had some type of comorbidity and half of the patients presented with a previous abdominal surgery (47%).

The 2 main indications for surgery were malignancy and diverticular disease (87.2%). Only one patient was treated for ulcerative colitis (UC), and included in those denominated as "others" were: 3 patients for non-acute volvulus, 5 for appendicular tumors, one for familial polyposis, and one for rectal prolapse.

With respect to the resected segment of the colon, the procedures for the left colon (left colectomy/sigmoidectomy/lower anterior resection) together represented 58% of the cases, and right hemicolectomy 25.8%. Only 3 total colectomies for UC and synchronous cancers were performed and only 2 exclusion procedures were carried out due to unresectable disease at the time of surgery.

Mean surgery duration was 181.44 min. It was not possible to make comparisons due to the important differences between conventional vs laparoscopic procedures or to the resected segment of the colon. The means of blood loss began at 100 ml, according to what was reported in the surgical notes.

In relation to postoperative treatment, the frequency of use of some measures known as risk factors for or protection against postoperative ileus were analyzed. A total of 62% of the patients were managed with peridural anesthesia during the procedure and practically all of the patients received postoperative analgesia that was based on opioids (tramadol) or NSAIDs.

A total of 19 (22.3%) of all the patients analyzed presented with prolonged postoperative ileus, when the first

**Table 1** Population characteristics.

Variable	Category	Frequency
Sex	Women	50
	Men	35
Age	Mean: 57.3 years (41.8-72.7)	
BMI	Obese patients (> 30 kg/m <sup>2</sup> )	22
Comorbidities	COPD	7
	DM	11
	HBP	19
	Previous abdominal surgery	40
ASA	ASA 1	53
	ASA 2	31
	ASA 3	1
Surgery indication	Malignancy	39
	Diverticular disease	35
	Inflammatory disease	1
	Others	10
Type of procedure	Right hemicolectomy	22
	Left hemicolectomy	22
	Sigmoidectomy	27
	Lower anterior resection	9
	Total colectomy	3
	Exclusion procedure	2
Approach	Laparoscopic	32
	Conventional	53
Mean surgery duration	181.44 min (106.2-256.64)	
Mean blood loss	110.06 ml (61.98-159.05)	
Peridural analgesia	Intraoperative analgesia	52
Postoperative opioids	Positive	41
Postoperative NSAIDs	Positive	46
Prolonged ileus	No prolonged ileus	66
	Prolonged ileus	19

passage of flatus or stool after the fourth postoperative day was used as the reference.

### Past surgical histories, comorbidities, and the presentation of prolonged postoperative ileus

The patients were divided into 2 groups in relation to the presence or absence of prolonged postoperative ileus. No statistically significant ORs were found for sex, comorbidities, ASA classification, past surgical history, or surgery motive.

Of this group of variables, the only one that had statistical significance was the presence/frequency of postoperative ileus in the obese patient, with an OR of 1.119 (0.015-1.230) and a *p* of 0.048. The data are summarized in [Table 2](#)

### The surgical event and presentation of prolonged postoperative ileus

In the analysis of risk factors in accordance with factors characteristic of the surgical procedure, no relevant OR was found with respect to the type of approach, the resected segment, surgery or anesthesia duration, mean opioid dose, or intraoperative blood loss or transfusions. Only

the perioperative use of peridural anesthesia presented with statistical significance with a *p* = 0.057 and OR of 0.363 (0.127-1.033), which was interpreted as a protective factor against prolonged postoperative ileus. The results are summarized in [Table 3](#)

### Postoperative follow-up and the presentation of prolonged postoperative ileus

Even though the present study is observational and non-interventional, some of the postoperative therapeutic strategies used in the sample were analyzed. No statistically significant relation was demonstrated between the use of a postoperative nasogastric tube, early parenteral nutrition, prokinetics, opioids, NSAIDs, or enoxaparin and the incidence of postoperative ileus. As was to be expected, admission to the acute ICU presented with an OR of 3.571 (0.952-13.392), with a statistically significant *p* of 0.050. The results are shown in [Table 4](#)

### Discussion and conclusions

The present study analyzed 25 potential predictors of prolonged postoperative ileus in patients that underwent

**Table 2** Past history, comorbidities, and presentation of prolonged postoperative ileus.

Variable	Ileus (n/%)	OR (95%CI)	p
<b>Sex</b>			
Men	12 (14.1)	0.435 (0.276-2.267)	0.435
Women	7 (8.2)		
<b>Age (years)</b>	61.8(55.7-67.9)		0.605
<b>ASA</b>			
I	12	0.956 (0.332-2.751)	0.934
II-III	7		
<b>Previous surgery</b>	11(12.9)	1.754 (0.625-4.925)	0.285
<b>COPD</b>	2 (2.3)	1.435 (0.256-8.061)	0.681
<b>Diabetes mellitus</b>	3 (3.55)	1.359 (0.323-5.724)	0.675
<b>High blood pressure</b>	6 (7.0)	1.882(0.601-5.894)	0.277
<b>Chemotherapy/radiotherapy</b>	1	0.356 (0.018-6.911)	0.495
<b>Obesity</b>	1 (1.7)	1.119 (0.015-1.230)	0.048
<b>Anemia (&lt;12 W, &lt;13 M)</b>	3 (3.5)	0.328 (0.087-1.242)	0.10
<b>Cause of the SX</b>			
Malignancy	12	1.687 (0.086-7.10)	0.09
Diverticulum	6	0.588 (0.199-1.738)	0.37
UC/Crohn's disease	0	1.11 (0.043-28.59)	0.945
Others	1	0.351 (0.04-2.96)	0.337

**Table 3** Surgical event and presentation of prolonged postoperative ileus.

Characteristic	Ileus (n/%)	No ileus (n/%)	OR (95%CI)	p
<b>Approach</b>				
Laparoscopic	3(3.5)	29(34.1)	2.378(0.782-7.232)	0.126
Conventional	16(18.8)	37(43.5)		
<b>Procedure</b>				
Right	7	15	1.98 (0.662-5.931)	0.220
Left	6	16	1.32 (0.572-3.051)	0.520
Sigmoidectomy	3	24	0.328 (0.086-1.242)	0.100
Lower anterior resection	0	9	0.375 (0.044-3.196)	0.678
Total colectomy	2	1	7.647 (0.653-89.432)	0.124
Exclusion	1	1	0.519(0.105-2.557)	0.342
<b>SX duration</b>				
> 180 min	8 (9.41)	35 (41.1)	1.552 (0.553-4.353)	0.403
<b>Anesthesia duration</b>				
>180 min	6 (7.05)	33(38.8)	0.875 (0.290-2.642)	0.814
<b>Morphine dose</b>				
Mean dose	21.1 (16.3-25.7)	23.9(21.3-26.4)		0.293
<b>Blood loss</b>				
>500 ml	3 (3.5)	5 (5.8)	2.288 (0.494-10.60)	0.290
<b>Transfusion in SX</b>	4 (3.5)	4 (5.8)	1.823 (0.307-10.815)	0.508
<b>Epidural anesthesia</b>	8 (9.4%)	11(12.94)	0.363 (0.127-1.033)	0.050



**Table 4** Postoperative follow-up and presentation of prolonged postoperative ileus.

Characteristic	Ileus (n/%)	OR (95%CI)	p
Admission to the acute ICU	5 (5.8)	3.571 (0.952-13.392)	0.050
Use of nasogastric tube	7 (8.2)	1.822(0.613-5.416)	0.279
Early total parenteral nutrition	5 (5.8)	1.022(0.416-2.511)	0.960
Prokinetics	7 (8.2)	2.378 (0.782-7.232)	0.126
Opioids	7 (8.2)	0.549 (0.192-1.568)	0.262
NSAIDs	9 (15.2)	0.750 (0.269-2.085)	0.581
Enoxaparin	2 (2.3)	0.519(0.105-2.557)	0.420

elective colon resection. However, the greatest limitation of our study was the small number of patients that met the inclusion criteria. In addition, we only presented the experience at a single center in which there was no standardized colon surgery service. But unlike other published studies, ours has the advantage of analyzing the incidence of postoperative ileus in different pathologies.

The analysis of the 85 study patients demonstrated a 22.3% frequency, which is slightly above that published by Chapuis et al.<sup>5</sup> (14%), Millan et al.<sup>6</sup> (15.3%), or Kronberg et al.<sup>7</sup> (10.2%). As mentioned above, there is no standardized definition of prolonged postoperative ileus among the studies evaluated, and it tended to be defined as the absence of the passage of flatus or stool between postoperative days 3 and 6.

One of the main goals of this protocol was to investigate the correlation of variables published as risk factors in other studies. Those variables include male sex, age, the need for intraoperative transfusion, the presence of pulmonary disease as a comorbidity, previous intra-abdominal surgery, the use of intraoperative opioids, blood loss, and a surgery duration longer than 3 h. In our case series of patients, only obesity (BMI  $\geq 30$ ) was found to be an independent discrete risk factor for prolonged ileus; OR 1.119 (0.015-1.230) and  $p = 0.048$ .

Several studies have demonstrated the benefits of laparoscopic surgery in relation to a reduced incidence of postoperative ileus in abdominal surgery.<sup>8</sup> No statistically significant relation between the results of our study and those published by Kuruba et al.<sup>9</sup> was found in the comparison of the 2 approaches. Nevertheless, only taking frequency into account, prolonged postoperative ileus presented more commonly in open procedures.

Analyzing the "prophylactic" measures utilized in our patient sample, the use of intraoperative peridural analgesia in colon surgery was shown to be a protective factor against the appearance of ileus with an OR of 0.363 (0.127-1.033) and a  $p = 0.057$ . Other commonly employed measures, such as nasogastric tubes, early parenteral nutrition, and prokinetics, did not demonstrate any benefit in relation to a reduced risk for ileus. None of the patients analyzed received chewing gum as a protective measure. Patient admission into the intensive care unit resulted in an increased risk of 3.5 with a  $p = 0.05$ , which should be interpreted with caution, because that population usually presents with various simultaneous adverse conditions.

The multifactorial etiology of prolonged ileus makes each patient different; the studies on risk factors only

calculate theoretical probabilities. It was concluded in the present study that obesity represented a risk factor for the appearance of prolonged postoperative ileus and the administration of peridural analgesia as a protective factor.

## Ethical responsibilities

**Protection of persons and animals.** The authors declare that no experiments were performed on humans or animals for this study.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

**Data confidentiality.** The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

## Financial disclosure

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## Conflict of interest

The authors declare that there is no conflict of interest.

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